

REMARKS/ARGUMENTS

The Office Action mailed October 18, 2004 has been carefully reviewed and the... foregoing amendments are made in response thereto. In view of the amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Claims 1-6 and 10-29 are currently pending. Claims 7-9 and 30-40 are canceled herein. Applicants have amended claim 1 to require that the array comprise probes for separately detecting a first and second RNA isoform from a target gene. Support for the amendments may be found in originally filed claim 31 and on page 18, lines 25-28 and page 23, lines 10-13 of the specification.

Objections to the Specification

In paragraph 4 the Examiner has objected to the specification and requests correction of the abstract and the priority claim. In response, Applicants have amended the abstract to give the uses of the claimed methods and amended the priority claim to correctly reflect the relationship between the instant application and the prior applications included in the application data sheet.

In paragraph 4 the Examiner also notes that trademarks are used in the application and should be capitalized. The specification has been amended to capitalize trademarks where included.

Claims Rejected Under 35 U.S.C §112, Second Paragraph

Claims 7-9 are rejected in paragraph 7 of the Office Action because the Examiner asserts that the metes and bounds of the phrases 3' region and 5' region are unclear. Applicants respectfully disagree but in an effort to advance the prosecution of the remaining claims, Claims 7-9 are canceled herein.

Claims Rejected Under 35 U.S.C §103(a)

Claims 1-4, 6-29 and 31-40 have been rejected over Lockhart et al. (US Patent No. 6,040,138) in view of Gibco BRL (Superscript™ Choice System for cDNA synthesis, Gibco BRL Catalog and Reference Guide, 1992) and Pharmacia Biotech (Molecular and Cell Biology Product Catalog, 1994), and further in view of Williams et al. (Nucleic Acids Research, Vol. 22, pages 1365-1397, 1994). Claim 5 has been rejected in view of these references and further in view of the Gibco catalog.

Lockhart *et al.* is cited for teaching a method of monitoring gene expression by hybridization of cDNAs derived from total RNA or mRNAs by reverse transcription using oligo dT primers and hybridization to high density arrays. The Gibco and Pharmacia catalogs are cited for teaching the use of random primers for cDNA synthesis. Williams et al. is cited for teaching that dangling ends of a duplex formed by the hybridization of two oligonucleotides has an unpredictable effect on the stability of the duplex. The Examiner asserts that one of skill in the art would have been motivated by Williams et al. to fragment the cDNAs before labeling to generate fragments that are similar to the lengths of the probes on the array to minimize dangling ends. The Gibco catalog is further cited for teaching the use of terminal transferase for labeling cDNA.

The amended claims are drawn to a method of analyzing an RNA sample comprising generating cDNA from the mRNA by hybridizing random primers to RNA, extending the random primers with reverse transcriptase, degrading the RNA population, fragmenting the cDNA, labeling the cDNA and hybridizing the fragments to nucleic acid probes on a solid support. The solid support comprises probes to separately detect different RNA isoforms from the same gene. Original claims 31 to 39 also taught methods for detecting the presence of different RNA isoforms in a sample by hybridizing the labeled cDNA fragments to arrays that comprise probes that can detect multiple isoforms and probes that detect individual isoforms. The Examiner did not address the additional limitations of claim 31-39 in the office action. Applicant asserts that none of the cited references teaches that the labeled cDNA fragments are hybridized to an array that comprises probes for separately detecting two different RNA isoforms from a target gene as required by the amended claims.

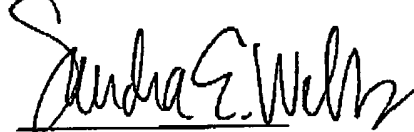
In summary, since the cited references, alone or in combination, do not teach or suggest the presently claimed invention, Applicants respectfully submit that the rejection of claims 1-6 and 10-29 under 35 U.S.C. §103(a) should be withdrawn.

Conclusion

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. Please deduct any additional fees from, or credit any overpayment to the undersigned's Deposit Account No. 01-0431. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5000.

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Respectfully submitted,



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